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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,682	04/27/2001	Rolf Bjerkvig	1702.401900	8676

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Patent Administrator
FMC Corporation
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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/763,682	BJERKVIG, ROLF	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12,14-17,19,20,24-28 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *12,14-17,19,20,26-28 and 32* is/are allowed.

6)☒ Claim(s) *24 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/05/04 has been entered. Claims 1-11, 13, 18, 21-23 and 29-31 have been cancelled. Claims 12 and 19 have been amended. Claims 12, 14-17, 19, 20, 24-28 and 32 are currently pending in the application and are addressed herein.

2. Applicant's arguments are addressed on a per section basis, as they apply to the presently pending claims. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 24 and 25 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. Preparing the microbeads by the dropwise addition of an alginate solution containing viable cells that express endostatin, angiostatin, thrombospondin or prolactin, to a calcium solution, critical or essential to the practice of the invention, but not

included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). Here the claims are drawn to a method for producing the composition described in claim 12. However, in order to make the composition of claim 12, there are two absolute requirements. First, the producer cell that is encapsulated by the alginate must be a cell that produces endostatin, angiostatin, thrombospondin or prolactin because claim 12 explicitly indicates that the encapsulated cell produces one of these CNS tumor inhibitors. Second, it is also required that the method of making the encapsulated cells include a step wherein 1-2% sodium alginate solution containing the producer cell is added in a dropwise manner to a 0.05-0.25M calcium chloride solution because the specification explicitly indicates:

> "A second advantage of the alginate matrices usable according to the present invention is that alginate microbeads prepared by the drop-wise addition of an alginate solution containing viable cells to a calsium solution, have a rising alginate concentration from the center of the microbead to the outer rim. Thereby an optimal space is created at the center of the microbeads for the cells to live, profilate and produce whereby sufficient nutrients and oxygen is available to the cells. The outer rim with its higher alginate concentration gives rise to a barrier, so that the producing cells inside the microbeads do not escape from the interior, nor do immunological cells enter into the beads." (see pp. 10-11); and
>
> " Sodium alginate is dissolved at a concentration of 1-2% in water or isotonic saline. The alginate solution is membrane sterilized and the producer cells are then added and isotonicity adjusted. Calcium alginate beads are formed by dripping the sodium alginate producer-cell solution into a bath of calcium chloride (0.05-0.25M)" (see pp. 11-12)

Therefore, it is essential that in order to make the microbead having an increasing G concentration from the center to the outer rim of the microbead the alginate solution must be a 1-2% sodium alginate solution, and the sodium alginate-producer cell solution MUST be added in a dropwise manner into a solution of 0.05-0.25M calcium chloride. Without these two essential elements in the claim, one of ordinary skill in the art would not know how to make the claimed microbead that contains a producer cell that produces endostatin, angiostatin, thrombospondin or

prolactin and that has an increasing G concentration from the center of the microbead to the outer rim of the microbead without performing an undue amount of additional experimentation.

Response to Arguments

5. Applicant's arguments, see pages 5-7 of the response filed 4/5/04, with respect to the rejection(s)of claim(s) under 35 USC 103 have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of in view of the additional limitation that the G concentration increases from the center of the microbead to the outer rim (see above rejection).

6. With respect to the rejection of claims under 103, applicants' arguments that the cited prior does not teach the limitation that the G content increases from the center of the bead to the outer rim is correct. It is acknowledged that a prior art reference of record (Smidsrod and Skjak-Braek, TIBS 1990) does teach a method for making encapsulated producer cells wherein the G concentration increases from the inner part to the outer part of the microbead. Smidsrod indicates that making the encapsulated cell by adding sodium solution containing the producer cell to a solution of Calcium chloride in a dropwise manner will make such a microbead. However, there is no indication in Smidrod that the producer cell produces any of the claimed CNS tumor inhibitor (endostatin, angiostatin, thrombostatin or prolactin). Although other references teach encapsulated cells that produce anti-CNS tumor products (such as FasL) there is no teaching of a microbead containing a producer cell that produces endostatin, angiostatin, thrombospondin or prolactin wherein the microbead has an increasing concentration of G from the inner most part of the bead to the outer most part found in the prior art. As such, the claimed

invention would not have been obvious to one of ordinary skill in the art at the time the invention was made. Nor would there have been an expectation of success to combine what was known in the prior art to make the claimed invention. Therefore, the 103 rejection has been withdrawn in view of the amended claims.

Allowable Subject Matter

7. Claims 12,14-17,19,20,26-28 and 32 are allowed. For the reasons indicated above.

Conclusion

Claims 24 and 25 are rejected for the reasons indicated herein, but should they be amended to include the essential elements indicated, the claims would be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (571) 272-0756. The examiner can normally be reached on M-F (8:00-5:30) with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DAVE T. NGUYEN
PRIMARY EXAMINER

Jon Eric Angell, Ph.D.
Art Unit 1635